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25 Hydroxy Vitamin D Levels In Patients Of Chronic Obstructive Pulmonary Diseases

Medicine

KEYWORDS: Vitamin D, COPD

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ABSTRACT

This study was conducted to assess the levels of 25 OH vitamin D in patients of COPD, to check the correlation between vitamin D levels and FEV1/FVC ratio and to know the association of vitamin D levels and the staging of COPD as per GOLD guidelines. Sixty patients of COPD and fifty-five healthy age matched control were included. Serum 25 hydroxy vitamin D was measured. Levels < 10ng/ml was considered as deficient and 10-30ng/ml as insufficient. More number of COPD patients had Vitamin D deficiency and insufficiency. Patients with lower levels of vitamin D had lower FEV1, lower FEV1/FVC ratio, higher smoking index and a higher Gold staging of 3-4. There was no significant correlation between BMI and Vitamin D. Patients of COPD are at risk of vitamin D deficiency and insufficiency with a significant association between smoking index and lung function. Vitamin D levels should be checked in all patients of COPD.

Introduction

COPD is now considered to be a systemic disorder with multisystem involvement which along with the comorbidities poses a challenge to the treating physician. There is a marked variation in prevalence of this disease and it has been ranked sixth as a cause of death in 1991 with an estimation of becoming third by 2020. The association of comorbidities has a significant impact on the morbidity of the patient. Comorbidities like hypertension, osteoporosis, chronic renal failure, heart failure, diabetes, ischemic heart disease, anemia and polycythaemia have been found to be associated with COPD. One of the often underdiagnosed major comorbidities is osteoporosis which is associated with poor health status and poor prognosis. Vitamin D has been known to play a major role in preserving the skeletal well-being. Studies have shown the association of lower levels of vitamin D with reduction of lung functions. Very few studies have been conducted to know the prevalence of vitamin D in COPD and its correlation with the severity of disease. The aim of the present study was to compare the level of vitamin D in COPD patients as compared to controls and also to study the association of vitamin D with the staging of COPD as per Gold guidelines.

Methods

We studied 25 OH vitamin D levels in COPD patients and if they are associated with FEV1/FVC ratio COPD Stage as per GOLD guidelines. This case-control study included 60 patients of COPD presenting in the outpatient and inpatient of Department of Chest & TB, Govt. Medical College, Patiala and 55 healthy age matched controls from amongst the relatives of patients. An informed consent was taken from all patients and controls and the study protocol was approved by the ethics committee of the institution. Patients having any comorbid conditions like diabetes, carcinoma, deranged renal or liver functions and a history of vitamin D supplementation were excluded.

The diagnosis of COPD was based on history, clinical presentation, radiological findings on X-ray chest and spirometry. Spirometry measuring FEV1, FVC and FEV1/FVC ratio were measured using Spiro Air, Medisoft. All the spirometry manoeuvres were performed according to the guidelines of the American Thoracic Society. The post bronchodilator spirometry was performed in all patients after administration of an adequate dose of short acting inhaled bronchodilator i.e 400 micro grams of levo-salbutamol. The presence of post-bronchodilator FEV1/FVC <0.70 confirmed presence of airflow limitation and COPD. Based on post bronchodilator FEV1/FVC and FEV1, patients were categorised into four stages of COPD – Mild COPD (FEV1/FVC < 0.70, FEV1 > 80% predicted); Moderate COPD (FEV1/FVC < 0.70, 50% < FEV1 <80%); Severe COPD (FEV1/FVC <0.70, 30% < FEV1 <50% predicted); Very severe COPD (FEV1/FVC < 0.70, FEV1 < 30% predicted or FEV1 <50%predicted plus chronic respiratory failure).

For assessment of 25 OH vitamin D, 2 ml blood was drawn under aseptic conditions, serum extracted and and evaluated using ELISA. An intense debate is going on to regarding the optimal levels of Vitamin D and the level of Vitamin D deficiency. Most experts now agree that vitamin D deficiency should be defined as a 25(OH)D of < 20 ng/ml. Vitamin D insufficiency is now recognized as a 25(OH)D of 21-29 ng/ml. The preferred level for 25(OH) D is now recommended by many experts to be > 30 ng/ml. For this study we categorised Vitamin D levels were categorised as deficient (<10 ng/ml), Insufficient (10-30 ng/ml) or normal (>30 ng/ml). All cases or controls with vitamin D deficiency were given free supplements for a period of 6 weeks.

Data analysis was performed using SPSS (Statistical Package For Social Sciences). Mean ± SD were used for descriptive analysis of the quantitative data and frequencies and percentages for descriptive analysis of qualitative data. Inferential analysis was done using Student's 't' test and Chi square tests respectively. Statistical significance was used as conventional 5% ($p<0.05$).

Results

The characteristics of the study population are shown on table1. Overall males were more than females. Controls were about 4 years younger than cases. All the controls were non-smokers while there was only one non-smoker in cases. There was a statistically significant difference between FEV1, FVC & FEV1/FVC ratio of cases and controls [Table1]. Cases had a significantly lower Vitamin D levels than controls [Fig1].

Only 8.3% cases had sufficient vitamin D levels as compared to 72.7% in controls. The cases had a significantly higher number of Vitamin D deficient or insufficient cases as compared to controls [Table1]. Vitamin D was significantly associated with FEV1/ FVC ratio (Pearson's r=0.699, p<0.001) and FEV1 (Pearson's r=0.744, p<0.01) i.e. those with higher vitamin D levels tend to have better FEV1/FVC and FEV1. There was significant negative correlation between Smoking Index and Vitamin D Levels among cases and controls (Spearman's rho = - 0.707, p<0.001) i.e. as the smoking index increases, Vitamin D levels tend to decrease (Table/fig 5). Also, age showed a significant negative correlation with Vitamin D levels (Spearman's Rho = 0.303, p=0.001) i.e. higher age groups had lesser vitamin D levels. This could be a confounding factor in or study.

Discussion

Lower Vitamin D has been shown to be associated with faster decline in lung function and with a higher risk of COPD in prospective analyses. It has been reported that vitamin D deficiency correlates with severity of COPD. It has also been observed that COPD patients had a raised risk for vitamin D deficiency. Moreover systemic side effects of COPD have become a matter of concern and this disease is now being called a systemic disease . A viewpoint of naming COPD to chronic systemic inflammatory syndrome was also put by some authors.

In this study, the levels of Vitamin D levels were significantly decreased as compared to controls which is consistent with the previous studies .

In the present study, the correlation of vitamin D levels with FEV1/FVC was found out to be a significant positive correlation (Pearson's r=0.556, p<0.001) i.e. those with higher vitamin D levels tend to have better FEV1/FVC. There was also a significant positive correlation between Vitamin D levels and FEV1 (Pearson's r=0.616, p<0.001) i.e. those with higher vitamin D levels tend to have better FEV1. Dose response relationship between Vitamin D and FEV1 and a positive relationship between serum 25(OH)D concentrations and FEV1 was also observed in other studies. These findings signify that sufficient levels of serum 25(OH) D in patients with COPD exert beneficial effects on patency of airways and lead to pulmonary function improvement. Zendedel et al conducted a study in which the case group received 100,000 IU of oral vitamin D per month, for 6 months than the placebo group. This study showed a significant differences in FEV1 and the number of COPD exacerbations between the study and placebo group patients with an increase in FEV1 was increased and reduction in COPD exacerbations.

Smoking index and Vitamin D levels showed a significant negative correlation cases and controls (Spearman's rho = -0.436, p<0.001) i.e. as the smoking index increases, Vitamin D levels tend to decrease. Smoking is a known risk factor for vitamin D deficiency and the vitamin D deficiency increases with increasing pack years. This was shown in earlier studies as well. It has been shown that cigarette smoking decreases the production of active form of vitamin D in lung epithelial cells. Cigarette smoke may also affect expression levels of vitamin D receptors.

In the current study it was found that as the GOLD stages increases the levels of vitamin D decrease as has been shown in previous studies.

Aging skin, poor storage capacity of fat due to wasting and poor diet can be another reasons for lower levels of vitamin D in patients of COPD. Vitamin D also affects lung functions as has been shown in this and previous studies. Various innate and adaptive mechanisms are implicated in the pathogenesis. Cells of adaptive immunity express receptors for vitamin D and require it for their optimal functioning. Maturation of dendritic cells and TH1 cells is also affected by lower levels of Vitamin D. Vitamin D also plays a role in protection from respiratory infections. The possible explanation is the increased expression of antimicrobial peptides and decrease of pro-inflammatory cytokines. All the above factors and a possible undiagnosed osteoporosis and decreased mobility of rib cage leads to a decline in pulmonary functions.

It has also been interpreted that Vitamin D3 supplementation protected against moderate or severe exacerbation, but not upper respiratory infection, in patients with COPD with baseline 25-hydroxyvitamin D levels of less than 50 nmol/L.

Limitation

Being a cross sectional study the cause and effect interpretation cannot be drawn. Also we did not study the diet pattern and the absence of data on dietary intake is a limitation of this study.

Conclusion

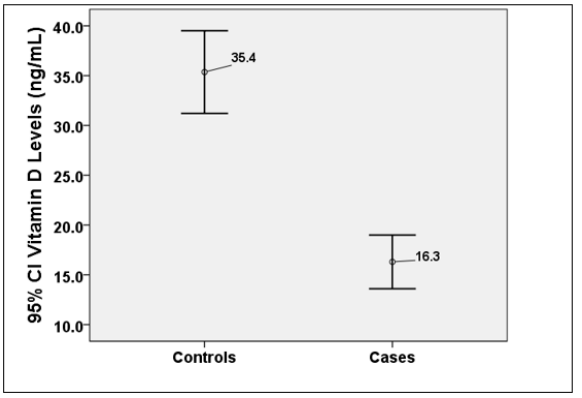
Vitamin D deficiency was observed in patients of COPD as compared to the age matched controls. The deficiency was found to be more in patients with higher pack years of smoking. It is recommended that vitamin D levels should be checked in patients of COPD especially poorly controlled patients of stage 3-4. Such deficiency should be treated to prevent osteoporosis, and fractures due to falls hence preventing morbidity and other multiple ill effects independent of COPD.

Table1:

Characteristics	Cases (n=60)	Controls (n=55)	p value
Age	62.7 ± 10.4	58.1 ± 8.4	0.011a
Male Gender	57 (95%)	50 (90.9%)	0.477 b
FEV1	41.1 ± 14.2	86.7 ± 4.5	<0.001 a
FVC	71.6 ± 19.0	90.8 ± 3.9	<0.001 a
FEV1/FVC	53.1 ± 14.7	93.9 ± 4.0	<0.001 a
Gold Staging Stage 0 Stage 2 (FEV1 50-80) Stage 3 (FEV1 30-50) Stage 4 (FEV1 <30)	00 (00.0%) 15 (25.0%) 28 (46.7%) 17 (28.3%)	55 (100.0%) 00 (00.0%) 00 (00.0%) 00 (00.0%)	-
Vitamin D	16.3 ± 10.4	35.4 ± 6.0	<0.001 a
Vitamin D deficiency categorised	31 (51.7%) 24 (40.0%)	0 (0.0%) 15 (27.3%)	-

a: Independent Sample t test; b: Fischer Exact Test; All values in parentheses are column-wise percentages

Fig1:



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